Maternal embryonic leucine zipper kinase is a key regulator of the proliferation of malignant brain tumors, including brain tumor stem cells.

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Public Summary:
Emerging evidence suggests that neural stem cells and brain tumors regulate their proliferation via similar pathways. In a previous study, we demonstrated that maternal embryonic leucine zipper kinase (Melk) is highly expressed in murine neural stem cells and regulates their proliferation. Here we describe how MELK expression is correlated with pathologic grade of brain tumors, and its expression levels are significantly correlated with shorter survival, particularly in younger glioblastoma patients. In normal human astrocytes, MELK is only faintly expressed, and MELK knockdown does not significantly influence their growth, whereas Ras and Akt overexpressing astrocytes have up-regulated MELK expression, and the effect of MELK knockdown is more prominent in these transformed astrocytes. In primary cultures from human glioblastoma and medulloblastoma, MELK knockdown by siRNA results in inhibition of the proliferation and survival of these tumors. Furthermore, we show that MELK siRNA dramatically inhibits proliferation and, to some extent, survival of stem cells isolated from glioblastoma in vitro. These results demonstrate a critical role for MELK in the proliferation of brain tumors, including their stem cells, and suggest that MELK may be a compelling molecular target for treatment of high-grade brain tumors.

Scientific Abstract:
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